UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,712	05/04/2001	Nobutaka Wakamiya	19036/37157	9190

7590 04/29/2003

Mark H Hopkins
Marshall O'Toole Gerstein Murray & Borun
6300 Sears Tower
233 South Wacker Drive
Chicago, IL 60606-6402

EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/29/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,712	WAKAMIYA, NOBUTAKA	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-96* is/are pending in the application.

4a) Of the above claim(s) *82-92,95 and 96* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-81,93 and 94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This is the First Office Action on the Merits of this U.S. National Stage application of the international application PCT/JP99/04552 filed 24 August 1999, which claims priority to Japanese patent application HEI-10-237611 filed 24 August 1998. The preliminary amendments A and B (Paper Nos. 8 and 9, respectively) filed 4 May 2001 have been entered. Claims 1-37 were canceled and claims 38-96 were amended in Paper No. 16. Claims 38-96 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I (claims 38-52 and 71-80) in Paper No. 15, filed 20 February 2003 is acknowledged.

Upon further consideration Groups I-III, VIII and IX will be rejoined with the elected Group I. Therefore, claims 38-81, 93 and 94 will be examined on the merits. Applicant's arguments for rejoinder of Groups IV-VIII and X, directed to an antibody that binds to fragments of SEQ ID NO:2 and methods of using said antibody and a transgenic non-human animal comprising a disrupted collectin homologue gene, are not persuasive.

The traversal is on three ground(s). First, Applicant requests that the restriction requirement be reconsidered in accordance with the International Preliminary Examination Report, wherein unity of invention was not found lacking. However, 37 CFR 1.499 states, "[i]f the examiner finds that a national stage application lacks unity of invention under § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Such requirement may be made before any

action on the merits but may be made at any time before the final action at the discretion of the examiner. Review of any such requirement is provided under § § 1.143 and 1.144." The examiner of the National Stage application is in no way bound by the findings of the International Search Authority.

Next, Applicant argues that the claims are linked in containing the single general inventive concept of SEQ ID NOS:1, 2, 4 and 5. This argument is not persuasive because claims directed to a polypeptide comprising SEQ ID NO:2 do not share the same special technical feature as claims directed to the antibody or methods of using the antibody. Although the antibody can bind to the polypeptide, the antibody is not limited to binding only a polypeptide comprising SEQ ID NO:2. The antibody is disclosed as capable of binding any collectin polypeptide or homologue thereof (e.g., see claim 90) and, it stands to reason, could be raised using any of the polypeptides to which it binds. Therefore the contribution which the antibody makes over the prior art extends well beyond its binding affinity for a protein comprising SEQ ID NO:2. Furthermore, the binding affinity of the antibody for collectin homologues demonstrates that the antibody is not limited by the particulars of SEQ ID NO:2 and therefore does not share the technical features of SEQ ID NO:2. Claims directed to a transgenic non-human animal comprising a disruption of the gene encoding a homologue of SEQ ID NO:2 clearly would not share a common special technical feature with the polypeptide encoding SEQ ID NO:2 because the disrupted gene does not encode SEQ ID NO:2 (i.e., it encodes a homologue of SEQ ID NO:2).

Finally, Applicant argues that the restriction would be improper even under U.S. practice because the examiner has not shown that it would be a serious burden to search and examine

Groups I-X together. Applicant argues that a search relating to the polypeptide of Group II would significantly overlap with the search required for the methods of screening, assaying, isolating or making the polypeptide or antibodies to the polypeptide. This argument is not persuasive because unity of invention, not U.S. restriction practice, applies in the instant case. Furthermore, the restriction is proper even according to U.S. restriction practice because the claims directed to the antibody, methods of using the antibody and animals comprising disruption of a homologue of SEQ ID NO:2 could not be searched coextensively with the polypeptide comprising SEQ ID NO:2 and therefore constitute an additional burden of search.

The requirement is still deemed proper and is therefore made FINAL.

Claims 82-92, 95 and 96 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The word "Novel" should be removed from the title, as it is redundant in the context of an issued patent. The remaining title "collectin" does not adequately describe the invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 38-81, 93 and 94 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. In order to comply with the utility requirement of 35 U.S.C. § 101, claimed subject matter must be supported by a disclosure of a specific, substantial and credible utility or by a well-established utility. In the instant case, the claims are directed to an isolated polypeptide having the amino acid sequence set forth as SEQ ID NO:2 (hereinafter referred to as the novel collectin) and fragments of said polypeptide. Additional claims are directed to polynucleotides encoding the novel collectin and fragments and homologues thereof, and vectors, host cells, animals and probes comprising the polynucleotide. On page 47, the specification sets forth the industrial applicability of the claimed invention as, "useful for investigating mechanisms of biological defense systems, and may provide medical, experimental tools in which biological activities of the novel collectin are utilized. For example, vectors that can express the novel collectin, host cells comprising the vector with feasibility of expression, antibodies for the novel collectin, as well as probes for screening the related molecular species of the novel collectin can be provided. In addition, transgenic non-human animals...are provided, which may be utilized as disease model animals for studies on functions, or regulation of expression of the novel collectin". The specification provides no teachings regarding the unique function of the novel collectin (i.e., those functions arising from its novel structure) and only vague statements regarding its role in host defense. As the specification provides no specific function for the protein and does not identify a single specific condition that could be diagnosed or treated according to the teachings of the specification, it fails to provide a specific utility for the claimed polypeptide, nucleic acid and transgenic animal. In fact, the asserted industrial applicability of the claimed Inventions is mostly directed to identifying the biological activity of

the novel collectin and then utilizing the claimed products to diagnose or treat diseases based on that biological activity, whatever it might be. This amounts to an invitation to the skilled artisan to experiment in order to discover the utility of the claimed invention. Therefore the utility provided in the specification is not substantial.

With regard to well-established utility, the specification generally teaches that the novel collectin might be involved in innate immunity based on homology to a family of proteins having Ca^{2+}-dependent carbohydrate recognition regions and collagen-like regions known as collectins. First, it should be pointed out that post-filing art clearly shows that the instant polypeptide comprising SEQ ID NO:2 occurs in nature as a membrane bound protein which has the activity of a scavenger receptor (see Ohtani *et al.* (2001) *J. Biol. Chem.* 276:44222-44228, Nakamura *et al.* (2001) *Biochim. Biophys. Acta* 1522:53-58 and Nakamura *et al.* (2001) *Biochem. Biophys. Res. Commun.* 280:1028-1035). The disclosure teaches only a fragment of the naturally occurring polypeptide which does not comprise the membrane spanning domain, and asserts that the disclosed polypeptide is functionally related to a family of soluble proteins. Clearly, the functional properties of the naturally occurring protein comprising SEQ ID NO:2 would be significantly different from the family of collectins, as they were understood at the time of filing, based simply on the fact that the instant polypeptide is membrane bound while collectins are known in the art as circulating, and in one instance intracellular, C-type lectins (see, for example, Hakansson *et al.* (2000) *Protein Sci.* 9:1607-1617). Although it is possible that the extracellular fragment of the naturally occurring novel collectin might have activity similar to a known collectin, the skilled artisan would not be able to identify a well established utility for the soluble portion of the novel collectin described in the application. Of the known collectins,

the sequence set forth as SEQ ID NO:2 is most homologous to SP-D, a collectin found in pulmonary surfactant capable of binding microorganisms and stimulating chemotaxis of phagocytes and production of oxygen radicals (see Hansen *et al.* (1998) *Immunobiol.* 199:165-189, especially the second full paragraph on page 166). However, SEQ ID NO:2 shares only 35% identity with SP-D over 304 amino acids. The art generally acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick *et al.* (2000) *Trends Biotechnol.* 18:34-39 teach that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating specific details of protein function (see Box 2, page 36). Similarly, Bork (2000) *Genome Res.* 10:398-400 teaches that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially page 399). Smith *et al.* (1997) *Nature Biotechnol.* 15:1222-1223 teaches, "[t]ypical database searching methods are valuable for finding evolutionarily related proteins, but if there are only about 1000 major superfamilies in nature, then most homologs must have different molecular and cellular functions" (second column on page 132). These teaching demonstrate the unpredictability of assigning protein function based on structure alone; and, given that the structural homology of the instant SEQ ID NO:2 to known collectins is 35%, at best, the function of the extracellular portion of the novel collectin described in the specification would be expected to be related to the function of other collectin family members in broad, general terms which do not suffice to assign a well-established utility to the claimed polypeptide.

For these reasons, claimed invention is not supported with a specific, substantial or well-established utility in accordance with the requirements of 35 U.S.C. § 101.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-81, 93 and 94 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 94 is additionally rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to

make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and breadth of the claims: The claim is directed to a transgenic non-human animal comprising a polynucleotide encoding a polypeptide having an amino acid sequence that comprises positions 229-547 of SEQ ID NO:2. The claims thus encompass any and all transgenic non-human animals comprising a recombinant gene that comprises said polynucleotide.

State of the prior art: With respect to how to use the instant claimed animal, the art teaches that the phenotype arising from insertion or deletion of even a well-characterized gene is unpredictable. Doetchman (1999) *Lab. Animal Sci.* 49:137-143 teaches, "[o]ne often hears the comment that genetically engineered mice...are not useful because they frequently do not yield the expected phenotype, or they don't seem to have any phenotype. These expectations are often based on years of work, and in some instances, thousands of publications of mostly in vitro studies" (page 137, paragraph 1). Doetchman goes on to teach, "it has become clear that genetic background plays an important role in the susceptibility of mice to many disorders. Therefore, the phenotypes of knockout mouse strains will also have genetic background dependencies" (page 140, column 2, third full paragraph) and "[a]pparent lack of phenotype more likely reflects or inability to ask the right questions, or our lack of tools to answer them" page 142, first paragraph. These teachings point out that the phenotype arising from any given mutation or genetic manipulation of a transgenic mouse is highly unpredictable and in some cases requires empirical experimentation to uncover. Therefore, the skilled artisan must rely on the prior art and disclosure to teach a useful phenotype for each and every transgenic animal.

Amount of direction provided by the inventor and existence of working examples: The teachings of the specification provide only a general recitation of how to make a transgenic mouse (Example 15). The disclosure does not provide a single example of a mouse, let alone all non-human animals made by the method. The teachings therefore do not provide a single phenotypic characteristic of the claimed animal such that the skilled artisan would know how to use the animal.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, given the art-recognized unpredictability of the phenotype arising from disruption of any given gene in any given animal, the skilled artisan would have to resort to trial and error experimentation in order to uncover a useful phenotype in the claimed animal. As there is no routine method with which the skilled artisan can identify or predict the phenotype arising from genetic manipulation of an animal, the level of experimentation required to use the claimed invention would clearly be undue.

Claims 38-81, 93 and 94 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The claims are directed to an isolated polypeptide having the amino acid sequence set forth as SEQ ID NO:2 and fragments of said polypeptide. Additional claims are directed to polynucleotides encoding the novel collectin and fragments and homologues thereof, and vectors, host cells, animals and probes comprising the polynucleotide. The claims thus encompass a genus of any and all nucleic acids and polypeptides comprising the disclosed nucleic acids and polypeptides, as well as products comprising said nucleic acids and polypeptides and methods of using said nucleic acids and polypeptides. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics (see MPEP 2163 (ii)). In the instant case, the claimed genus clearly encompasses species that were not in Applicant's possession at the time of filing. The post filing art cited above (i.e., Ohtani *et al.*; Nakamura *et al.*, *Biochim. Biophys. Acta*; and Nakamura *et al.*, *Biochem. Biophys. Res. Commun.*) demonstrates that the disclosed polynucleotide encodes a fragment of a membrane bound polypeptide expressed in humans that has the function of a scavenger receptor that is also capable of binding oxidized LDL. Although the claimed genus encompasses the naturally occurring membrane protein, the specification does not even remotely suggest a protein having the structural feature of a membrane spanning domain or the function of a scavenger receptor or capable of binding LDL. Clearly, therefore, the teachings of the specification fail to adequately describe the full scope of proteins and nucleic acids encompassed by the claimed genus.

Claims 53-56, 58-60, 66-68, 73-75, 78, 79 and 81 additionally lack adequate written description for a genus of polynucleotides which hybridize under stringent conditions with disclosed polynucleotides or with PCR amplification products obtained using the primers set forth as SEQ ID NO:4 or 5, and polypeptides encoded thereby, or for a probe comprising a polynucleotide according to claim 38. Although the claims specify stringent hybridization conditions, the specification provides only non-limiting examples of hybridization conditions considered to be stringent. Thus, according to the teachings of the specification, the stringency of the hybridization conditions, and therefore the homology of the nucleic acids identified to the disclosed nucleic acids could be low and the claimed polypeptides might be only distantly related to the disclosed polypeptide. Furthermore, as there is no limitation on the conditions under which the amplification product of claim 53 is produced, the nucleic acid of claim 53 is essentially unlimited in structure. That is, any nucleic acid that hybridizes under low stringency to a nucleic acid obtained from a low stringency PCR reaction is encompassed by the claims. The claimed genera of nucleic acids and polypeptides therefore encompass molecules having shared functional domains and only limited structural similarity. An adequate written description of a molecule requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the molecule itself. It is not sufficient to define molecule solely by its principal biological property (i.e., it encodes or is a collectin) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any molecule with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all molecules that achieve a result without

defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). With respect to the method claims, adequate description of the methods first requires an adequate description of the materials, i.e. specific molecules sequences, which provide the means for practicing the invention. With regard to claim 81, because the polynucleotide of claim 38 is not limited to a disclosed sequence (i.e., it comprises a disclosed sequence), a fragment of that sequence encompasses any and all nucleic acids. That is, a fragment of the nucleic acid comprised by the nucleic acid of claim 38 which does not consist of the sequence set forth as SEQ ID NO:1 could be any nucleic acid.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of nucleic acids and polypeptides encompassed by the claims. Therefore, only the polypeptide and nucleic acid sequences explicitly set forth in the disclosure meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 38-57, 71-81 and 93 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 98/55617 (published 10 December 1998; made of record in the IDS filed 19 February 2003; hereinafter '617).

The sequence set forth in '617 as SEQ ID NO:11 is identical to the polynucleotide claimed in claims 38-57. On page 14, line 5-6, '617 teaches a cDNA comprising SEQ ID NO:11 according to claim 57. Beginning the third paragraph on page 42 and continued through the second paragraph on page 43, '617 teaches vectors and host cells comprising the nucleic acid comprising SEQ ID NO:11 according to the limitations of claims 71-80; on page 45, paragraph 2, '617 teaches a probe comprising a fragment of the polynucleotide comprising SEQ ID NO:11 according to claim 81; and on page 43, paragraph 2, '617 teaches recombinant expression of the protein encoded by the polynucleotide comprising SEQ ID NO:11 according to claim 93. The polynucleotide, vector, host cell, probe and method taught in '617 are the same as those taught in the instant application; therefore, the limitations of the claims are met by '617.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
April 26, 2003

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER